

AMENDMENTS TO THE DRAWINGS

Please replace Figure 13 with the replacement sheet for Figure 13 submitted herewith.

REMARKS

1. Preliminary Remarks

a. Status of the Claims

Claims 1-70 are pending in this application, and claims 30-35 are under active consideration. Claims 1-29, and 36-70 have been withdrawn from consideration. Claims 1, 3, 5-10, 12-22, 24-27, 30, 32-35, 39, 47, 48, and 51-69 are amended; and claims 2, 4, 11, 23, 28, 29, 31, 36-38, 40-46, 49, 50, and 70 are canceled without prejudice to pursuing the canceled subject matter in a continuing application. Applicant hereby requests entry of the amendments and remarks made herein into the file history of the application. Upon entry of the amendments, claims 1, 3, 5-10, 12-22, 24-27, 30-35, 39, 47, 48, and 51-69 will be pending in this application; and claims 30 and 32-35 will be under active consideration.

b. Amendments to the Claims

Support for amended claims 1, 3, 5-10, 12-22, 24-27, 30, 32-35, 39, 47, 48, and 51-69 can be found throughout the application as originally filed. The claims are amended to relate to subject matter which Applicant thinks will expedite prosecution of this application. The claims are also amended to correct typographical errors and to correctly refer to Markush groups by using the either the term "selected from the group consisting of" or the term "or". Claim dependencies are amended for consistency.

c. Amendments to the Specification

The specification is amended to incorporate the substitute sequence listing submitted herewith by reference. The specification is also amended to replace the title with a title that describes the instantly claimed subject matter. The specification is further amended to add a heading for the Brief Description of the Drawings section that begins on page 53. The specification is also amended to identify the sequence disclosed in Figure 24.

d. Objections to the Specification

On pages 2 and 3 of the Office Action, the Examiner objects to the title of the application because it allegedly is not descriptive. The title has been amended to "METHOD FOR THE TREATMENT OF YB-1 POSITIVE TUMORS," which describes the claimed subject matter.

On page 3 of the Office Action, the Examiner objects to the lack of a heading for the descriptions of the drawings on page 53 of the specification. Page 53 is amended to add the section header, "BRIEF DESCRIPTION OF THE DRAWINGS" as requested by the Examiner. In view

of the foregoing, Applicant respectfully requests that the Examiner withdraw the objections to the specification.

e. Objection to the Drawings

On page 3 of the Office action, the Examiner objects to Figure 14 because it allegedly fails to show any details in the photograph of a mouse. Applicant thinks that the Examiner intended to refer to Figure 13, not Figure 14, since Figure 13 depicts a Southern blot while Figure 14 is a photograph of mice. Submitted herewith is a replacement sheet for Figure 13, which Applicant submits better shows the details of the photograph of the mice. In view of the foregoing, Applicant respectfully requests that the Examiner withdraw the objection to the drawings.

f. Sequence Compliance

On pages 3 and 4 of the Office Action, the Examiner alleges that the application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825. Specifically, the Examiner asserts that Figure 24 contains a sequence that is not identified by a sequence identifier. Submitted herewith is a substitute sequence listing that includes the sequence disclosed in Figure 24. The brief description of this figure is amended to refer to its identifier SEQ ID NO: 16.

g. Objections to the Claims

On page 4 of the Office Action, the Examiner objects to claims 30-35 because the allegedly do not begin with an article. The Examiner also objects to claim 30 because the descriptions of the viral oncogene are allegedly grammatically incorrect. Amended claim 30 refers to “an isolated adenovirus,” and amended claims 32-35 refer to “the adenovirus.” Parts (a) and (b) of amended claim 30 have verbs as required by the Examiner. In view of the foregoing, Applicant respectfully requests that the Examiner withdraw the objections to the claims.

2. Patentability Remarks

a. 35 U.S.C. § 101

On pages 4 and 5 of the Office Action, the Examiner rejects claims 30-35 under 35 U.S.C. §101 as allegedly being drawn to non-statutory subject matter. The Examiner asserts that the instant claims do not sufficiently distinguish over cells that exist naturally because the claims do not particularly point out any non-naturally occurring products. As suggested by the Examiner, amended claim 30 refers to an isolated adenovirus.

In view of the foregoing amendments, Applicant submits that the rejection is hereby rendered moot as the claims are directed to subject matter created by the hand of man and thereby is statutory subject matter. *See, e.g., Diamond v. Chakrabarty* 447 U.S. 303 (1980). Accordingly,

Applicant respectfully submits that the rejection of claims 30-35 under 35 U.S.C. § 101 has been overcome and should be withdrawn.

b. 35 U.S.C. § 112, second paragraph

On page 5 of the Office Action, the Examiner rejects claim 32-35 under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. The Examiner asserts that the limitations, “deletion of the CR3 region, deletion of the N-terminus and deletion of the C-terminus,” and “the wild-type,” lack antecedent basis. Amended claim 32 replaces the aforementioned uses of the term “the” with the term “a” and has deleted the phrase “the wild type,” thereby rendering the rejection moot. In view of the foregoing, Applicant respectfully requests that the rejection of claims 32-35 under 35 U.S.C. § 112, second paragraph, has been overcome and should be withdrawn.

c. 35 U.S.C. § 112, first paragraph

On pages 6-9 of the Office Action, the Examiner rejects claims 30-35 under 35 U.S.C. § 112, first paragraph as allegedly lacking sufficient written description. The Examiner asserts that the claimed E1A mutations are not structurally limited to specific mutations, specifically because the claimed mutations and deletions are not limited in size. The Examiner further asserts that the claims encompass an enormous number of E1A oncogenes. Applicant respectfully disagrees.

Amended claims 30 and 32-35 are directed to an adenovirus capable of only replicating in a cell where YB-1 is present in the nucleus. Applicant submits that specific mutations and deletions within the E1A gene had been pinpointed to transactivation activity of E1A at the time of filing. For example, Jelsma *et al.*, *Virol.* 163:494-502 (1988), Wong *et al.*, *J. Virol.* 68:4910-4920 (1994)(of record), and Glenn *et al.*, *J. Virol.* 56:66-74 (1985) together teach a series of E1A protein mutants that retained transactivating activity including (a) deletion of the CR3 region (amino acids 140-185), (b) point mutations in the CR3 region such as at amino acid residues 173 and 176, (c) deletions in the CR1 region (amino acid residues 20 to 67) alone or in combination with CR3 point mutations at amino acid 173 and 176, and (d) deletion of the amino terminal end of the E1A protein (amino acids 3 to 25) either alone or in combination with deletion of amino acid residues 111-123. The specification itself points a number of E1A protein mutants that maintain transactivation activity on page 17 last paragraph to page 18 first paragraph; page 56, seventh full paragraph points to the Wong study discussed above; and Examples 1 and 5.

In view of what was known at the time of filing regarding E1A protein mutants retaining transactivation activity, and further disclosures of such mutations in the specification, Applicant submits that the specification and claims indicate distinguishing attributes shared by members of the

genus in order for one of skill in the art to reasonably conclude that the inventor had possession of the claimed invention at the time of filing. The issue is not whether E1A protein mutants with transactivation activity are described in the specification as one of skill would appreciate the breadth of this group of mutants, but rather whether one of skill would reasonably conclude that the inventor had possession of an adenovirus that is replication deficient in cells which lack YB-1 in the nucleus, but replicate in cells which have YB-1 in the nucleus. Applicant submits the specification clearly teaches such an isolated adenovirus and a standard screening of mutants of E1A could be generated to identify those adenoviruses having the characteristics of the claimed invention (i.e., a transactivating E1A protein supportive in the replication of adenovirus in a cell which has YB-1 in the nucleus, but unsupportive of replication of the adenovirus if YB-1 is not present in the nucleus.). In view of foregoing amendments and remarks, Applicant request that the written description rejection of claims 30-35 under 35 U.S.C. § 112, first paragraph, has been overcome and should be withdrawn.

d. 35 U.S.C. § 102

On pages 9 and 10 of the Office Action, the Examiner rejects claims 30-35 under 35 U.S.C. § 102 as allegedly being anticipated by US 6,649,158 ("LaFace" hereafter). The Examiner asserts that that LaFace discloses mutations in E1A that do or do not affect Rb binding. The Examiner further asserts that the E1A mutations of LaFace, given the alleged similarity to the instantly claimed deletions, results in a protein that mediate transactivation of E1B-55k and not YB-1 binding. Applicant respectfully disagrees.

Specifically, LaFace fails to appreciate isolating adenoviruses that are unable to replicate in a cell where YB-1 is not present in the nucleus, but can replicate in a cell where YB-1 is present in a nucleus and possesses particular E1A mutant proteins that support replication of the adenovirus via transactivation. Accordingly, LaFace does not teach or suggest the unique claimed invention. In view of the foregoing amendment and remarks, Applicant submit that the rejection of claims 30-35 under 35 U.S.C. § 102(b) has been overcome and should be withdrawn.

3. Conclusion

Applicant respectfully submits that the instant application is in good and proper order for allowance and early notification to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the instant application, the Examiner is encouraged to call the undersigned at the number listed below.

Respectfully submitted,

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